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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
DESAI, ANAND U	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 01/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/830,810	MATZUK ET AL.	
	Examiner	Art Unit	
	Anand U Desai, Ph.D.	1653	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 20 December 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☐ The a)☐ affidavit, b)☐ exhibit, or c)☐ request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *2,3 and 58-61*.

   Claim(s) withdrawn from consideration: _____.

8. ☒ The drawing correction filed on *25 July 2001* is a)☒ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

DETAILED ACTION

1. This Advisory action is in response to Amendment filed on December 20, 2004. Claims 1, 4, and 11-57 have been cancelled. Claims 2, 3, and 58-61 are currently pending and are under examination.

Withdrawal of Rejections

2. The rejection of claim 4 under 35 U.S.C. 112, second paragraph as being indefinite is withdrawn based on Applicant's amendment to cancel claim 4.

Maintenance of Objections and Rejections

Claim Objections

3. Claim 60 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 58. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 2, 3, and 58-61 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, and 2 of copending Application No. 10/475,502. Although the conflicting claims are not identical, they are not patentably distinct from each other because the current application claims an isolated polynucleotide sequence, O1-180, identified as SEQ ID NO:1, and copending Application No. 10/475,502 claims an isolated polynucleotide sequence encoding O1-180, identified as SEQ ID NO:11, and 13.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 2, 3, 5-10, and 58-61 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. The claims are directed to an isolated polynucleotide sequence designated as SEQ ID. NO: 1, an isolated polynucleotide that specifically hybridizes with SEQ ID NO:1, and an isolated polynucleotide that is either fully complementary to the polynucleotide of SEQ ID NO:1 or the isolated polynucleotide that specifically hybridizes with SEQ ID NO:1.

The specification does not specifically address the activity or use of the polynucleotide, SEQ ID. NO: 1. On page 2, line 30 the polynucleotide is suggested to function as other oocyte

specific genes. On page 3, starting at line 4 of the specification the polynucleotide is described in a general manner to relate to various cell proliferative or degenerative disorders, and infertility. On page 3, beginning on line 16, the specification describes the use of the polynucleotide as a reagent to study ovarian development and function. The specification also discloses that the polynucleotide can be used to screen for genetic mutations in components of signaling pathways that are associated with some forms of human infertility or gynecological cancers. On page 3, beginning on line 25 the polynucleotide is suggested to be used in the generation of mutant mice for the further study of oogenesis and/or folliculogenesis. The knockouts are suggested to provide key insights into the roles of the polynucleotide gene product in human female reproduction. On page 7, beginning on line 1, the specification states that based on the known activities of many other ovary specific proteins, it can be expected that the protein product from the polynucleotide will also possess biological activities that will make them useful as diagnostic and therapeutic reagents. On page 7, beginning on line 5, the specification suggests that based on similar expression patterns of the claimed novel polynucleotide and a growth differentiation factor-9, the protein product of the polynucleotide would function in a similar manner. On page 7, beginning on line 14, the specification suggests that since the protein product of the polynucleotide has similar tissue of origin as inhibin, both would possess similar biological activities. On page 7, line 23, the specification discloses that the protein of the polynucleotide may be useful as an indicator in prenatal screening procedures. On page 7, beginning on line 25, the specification suggests that the protein of the polynucleotide may function for the treatment of ovarian cancer. On page 19, beginning on line 2, the specification suggests that sequences complementary to the polynucleotide sequence claimed

could be used in treatments of cell-proliferative disorders. On page 20, line 5, the specification teaches the use of the polynucleotide in gene therapy. On page 23, line 15, the specification states that the protein product of the polynucleotide could play a role in regulation of the menstrual cycle, and therefore, could be useful in various contraceptive regimens. On page 28, beginning on line 18, the specification discloses that the open reading frame of the polynucleotide product fails to demonstrate any structural motifs reminiscent of known proteins, suggesting that they will be functionally unique.

These are not considered to be specific or substantial utilities for the polynucleotide. The method such as recombinant production of protein is not considered to be specific or substantial utility. These asserted utilities are broad and are not specific to the polynucleotide of SEQ ID. NO: 1. There is no disclosed signaling pathway associated with the polynucleotide of SEQ ID. NO: 1, and there is no disease or disorder correlated with the polynucleotide of SEQ ID. NO: 1. For example, on page 19, the passage does not disclose which cell-proliferative disorders will be treated with the polynucleotide of SEQ ID. NO: 1. Given that the specification does not disclose how to use the polynucleotide, a skilled artisan would not know how to use the polynucleotide or a polynucleotide that hybridizes with it. Thus, the specification fails to set forth a specific and substantial utility.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2,3, 5-10, and 58-61 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Response to Applicant's Remarks

Applicants traverse the rejections of claims 2-10 under 35 USC § 101, and § 112. Applicants state the Patent Office did not properly establish a *prima facie* case of lacking utility. Applicants state that the specification defines SEQ ID NO:1 as a polynucleotide, which modulates fertility. Applicants further state that the response filed on July 14, 2004 provided further evidence which confirmed that SEQ ID NO:1 effects fertility. Applicants assert that they have provided documentary evidence, which the Examiner appears to have overlooked. Particularly, the Wu et al. publication establishes that Zar1 homozygous knockout mice ($Zar^{-/-}$) are infertile, and Zar1 and SEQ ID NO:1 are similar polynucleotides, thus the present invention has utility, in that it has a "real world" use or application in the world of fertility.

Applicant's remarks filed on December 20, 2004 have been thoroughly reviewed and considered, but is insufficient to overcome the rejection of claims 2-10, and 58-61 based upon lack of utility and/or inoperativeness under 35 U.S.C. 101 and 112, 1st paragraph as set forth in the last Office action because they are not found persuasive for the following reasons:

Initially, so as to remove any confusion on the part of the Applicant, the identification of a signaling pathway, disease, or disorder associated with the polynucleotide of SEQ ID. NO:1

was merely suggested as a means of establishing a specific and substantial utility, not a requirement for establishing a specific and substantial utility.

The 35 U.S.C. 101 rejection in the previous office action mailed April 21, 2004 and October 18, 2004 clearly sets forth the reasoning used in concluding that the asserted utility for the claimed invention is neither specific and substantial or a well established utility. The method such as recombinant production of protein is not considered to be specific or substantial utility. These asserted utilities are broad and are not specific to the polynucleotide of SEQ ID. NO: 1. The suggestion that a similar expression pattern confers similar function is not convincing. In addition, example 7 in the specification appears to describe further research that can be performed to identify a function of the protein encoded by the isolated polynucleotide of SEQ ID NO:1.

Further, the publication submitted in support of a specific and substantial or a well established utility, which was published in January of 2003 states that identification of proteins that interact with Zar1 may provide insights into the role of Zar1 (SEQ ID NO:1) in regulating the transition from oocyte to embryo (see page 190, last sentence before METHOD section), which is indicative of further experimentation for characterization of a protein encoded by the isolated polynucleotide identified as SEQ ID NO:1. Thus, the specification still fails to set forth a specific and substantial utility for the isolated polynucleotide sequence designated as SEQ ID. NO: 1, an isolated polynucleotide that specifically hybridizes with SEQ ID NO:1, and an isolated polynucleotide that is either fully complementary to the polynucleotide of SEQ ID NO:1 or the isolated polynucleotide that specifically hybridizes with SEQ ID NO:1.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 58-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. The term "specifically hybridizes" in claims 58 and 60 is a relative term, which renders the claim indefinite. The term "isolated polynucleotide" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. What are the conditions, the temperature, and concentration of salt in a hybridization buffer, for a polynucleotide that specifically hybridizes? Suggest, "..that specifically hybridizes under conditions of 0.015 M NaCl at a temperature of 60°C with the polynucleotide of claim 2."

11. Claims 59, and 61 are rejected for depending on a rejected claim.

Response to Applicant's Remarks

Applicants traverse the rejection of claims 2-10 and 58-61 under 35 U.S.C. § 112, second paragraph. Applicants assert that the term "specifically hybridizes" is not relative and does not render the claim indefinite.

Applicant's remarks filed on December 20, 2004 have been thoroughly reviewed and considered, but is insufficient to overcome the rejection of claims 58, and 60 under 35 U.S.C. 112, 2nd paragraph as set forth in the last Office action because they are not found persuasive for the following reasons:

The phrase "specifically hybridizes" is not definite, it cannot be determined what conditions are necessary for the instant invention because the specification, particularly on page 11, lines 22-25, does not define what is considered "stringent."

Conclusion

12. No claims are allowable.

A shortened statutory period for reply to the FINAL action is set to expire THREE MONTHS from the mailing date of the FINAL action. In the event a first reply is filed within TWO MONTHS of the mailing date of the FINAL action and the Advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of the FINAL action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 9:00 a.m. - 5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (517) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

December 28, 2004

JON WEBER
SUPERVISORY PATENT EXAMINER